REMARKS

Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the remarks and amendments herein.

I. STATUS OF TH E CLAIMS AND FORMAL MATTERS

Claims 1, 5-7, 10-36 and 41-43 are now pending. Claims 1, 5 and 10 have been amended, and claims 2-4, 8-9 and 37-40 have been canceled, without prejudice, without admission, without surrender of subject matter and without any intention of creating any estoppel as to equivalents.

No new matter is added.

It is submitted that these claims are and were in full compliance with the requirements of 35 U.S.C §112. In addition, the amendment and remarks herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§101, 102, 103 or 112; but rather the amendments and remarks herein are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Support for the amended claims is found throughout the specification and the originally filed claims, and specifically in original claims 4 and 9.

II. THE CLAIM OBJECTIONS ARE OVERCOME

Claim 5 was objected to as being of dependent form for allegedly failing to further limit the subject matter of a previous claim. Claim 5 previously depended on claim 4, however the amendment herein has canceled claim 4 and added the recitation of claim 4 into claim 1, such that claim 5 now depends on claim 1. It is believed that the objection to claim 5 is still pertinent, such that it is addressed herein.

Claim 1 recites that "the apoptosis inducer is a tumour necrosis factor apoptosis inducing ligand (TRAIL)". Claim 5 further limits claims by requiring that "the TRAIL is TRAIL/Apo-2L". The Office Action states that this is improper because TRAIL and Apo-2L are the same cytokine. Applicants respectfully disagree.

It is respectfully submitted that claim 1 recites that the apoptosis inducer is a TRAIL. Simply, claim 1 indicates that the apoptosis inducer is a molecule that is a tumour necrosis factor apoptosis inducing ligand; in other words, claim 1 contemplates that there exist molecules that are other than Apo-2L are a tumour necrosis factor apoptosis inducing ligand. Therefore, claim 5 further limits

claim 1 by reciting a specific tumour necrosis factor apoptosis inducing ligand, namely Apo-2L, as opposed to the general class of tumour necrosis factor apoptosis inducing ligands.

Accordingly, claim 5 properly provides a further limitation to claim 1, such that the dependency of claim 5 on claim 1 is proper. Therefore, reconsideration and withdrawal of the objection to claim 5 is respectfully requested.

III. THE DOUBLE PATENTING REJECTIONS ARE OVERCOME

Claims 1-3 and 8-32 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,676,934. Applicants respectfully traverse.

The amendments herein have inserted the recitation that the apoptosis inducer is a tumour necrosis factor apoptosis inducing ligand (TRAIL) into independent claim 1. This recitation was originally found in claim 4, which was not subject to the double patenting rejection.

Accordingly, the insertion of this recitation in claim 1 is respectfully believed to distinguish claim 1, and all claims dependent on claim 1, from U.S. Patent No. 6,676,934 such that the rejection is now moot. Therefore, reconsideration and withdrawal of the double patenting rejections is respectfully requested.

IV. THE WRITTEN DESCRIPTION REJECTIONS ARE OVERCOME

Claims 1-36 and 41-43 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the invention at the time of filing. The rejection is respectfully traversed.

The Office Action stated that the present application teaches that EMATE, 2-EtEMATE, 2-MeO EMATE, and 2-MeO2bis EMATE are highly potent in preventing and/or inhibiting growth of breast cancer cells as well as the cytokine TRAIL, an apoptosis inducer, but that the specification does not disclose all sulphamates and apopotosis inducers.

The amendments to the claims herein now require that the sulphamate is a polycyclic compound and that the apoptosis inducer is a tumour necrosis factor apoptosis inducing ligand. It is respectfully submitted that these recitations are sufficiently descriptive, and are sufficiently

described within the specification, such that one of skill in the art would understand that the inventors had possession of the invention at the time of filing. Indeed, the term "polycyclic sulphamate compound" has previously been considered to have sufficient written description, for example, as in U.S. Patent 6,676,934. In U.S. Patent 6,676,934, as in the present application, the compounds specifically described in the specification and the examples were primarily analogs of EMATE. However, the issued claims recited a "polycyclic sulphamate compound", and in issuing the claims, the Patent Office asserted that the term did not suffer from a lack of written description. The same must then be true of the present application.

Additionally, it is respectfully submitted that the recitation that the apoptosis inducer is a tumour necrosis factor apoptosis inducing ligand is likewise sufficiently described.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, are respectfully requested.

V. THE ENABLEMENT REJECTIONS ARE OVERCOME

Claims 1-36 and 41-43 were also rejected under 35 U.S.C. §112, first paragraph, as allegedly being non-enabled for a composition comprising a non-steroidal sulphamate compound and any apoptosis inducer, a non-steroidal sulphamate compound and TRAIL, or a steroidal sulphamate compound and any apoptosis inducer. In addition, claims 32-36 and 41-43 were rejected under 35 U.S.C. §112, first paragraph, as allegedly being non-enabled for a method of treatment of a subject with EMATE, 2-MeO EMATE, 2-EtEMATE or 2-MeO2bis EMATE and TRAIL. The rejections are respectfully traversed and will be addressed in turn.

Initially, the claims have been amended herein such that claim 1 now specifies that the sulphamate compound is a polycyclic compound and the apoptosis inducer is a tumour necrosis factor-related apoptosis inducing ligand (TRAIL). Accordingly, it is respectfully submitted that the claims do not call for the use of any apoptosis inducer. As such, the claims are now enabled as to the apoptosis inducer, such that the enablement rejection as to this term is now moot and should be withdrawn.

Turning now to the enablement rejection based on the claims reading on non-steroidal sulphamate compounds, the Examiner is respectfully invited to review the present specification at page 20, line 16 to page 21, line 1. The specification therein provides a non-steroidal skeletal structure for compounds that are suitable for use in the present invention. Furthermore, the

claims as amended herein now require that the sulphamate compound be a polycyclic compound. Applicants respectfully submit that the teachings of the office action are sufficient to enable the presently amended claims.

The Examiner's attention is respectfully directed to *In re Wands*, 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988), wherein the Federal Circuit stated at 1404 that:

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. 'The key word is undue, not experimentation.' The determination of what constitutes undue experimentation in a given case requires the application of standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed ... [Citations omitted].

Against this background, determining whether undue experimentation is required to practice a claimed invention turns on weighing the factors summarized in *In re Wands*. These factors include, for example, (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims; all of which must be taken into account.

The Office Action admits that the level of skill in the art is high, but states that it is not predictable the any sulphamate compound would have the same activities as the EMATE analogs specifically exemplified in the specification. As described above, the claims have been amended herein, such that the sulphamate compound must be a polycylic compound. Further, the specification provides examples of both steroidal and nonsteroidal polycyclic compounds that can be used in practice of the invention. Accordingly, the skilled artisan is not without sufficient guidance to select compounds which can be used with a TRAIL to practice the invention. Therefore, the quantity of experimentation required to practice the invention would be low as a result of the high level of skill in the art, the state of the prior art, specifically the large quantity of knowledge that exists as to compounds that are useful in the treatment of cancers, the

significant amount of guidance provided in the specification, and the breadth of the claims. Applicants respectfully submit that the introduction of polycyclic compound recitation into claim 1 provides imparts into the claim a reasonable generalization of the examples such that limitation of the claims to a more narrow scope with deny the Applicants fair protection for their invention.

Accordingly, as it is respectfully submitted that undue experimentation would not be necessary to practice the invention as currently claimed, reconsideration and withdrawal of the enablement rejection is respectfully requested.

Turning now to the rejection of the method of treatment claims, the Office Action states that the specification is not enabled for method of treatment claims in the face of a lack of working examples and references by Gura and Rakesh which state that human cancer cells *in vitro* are poor representatives of malignancy *in vivo*. Applicants respectfully disagree.

According to the present Office Action, in order to obtain claims directed towards a method of treatment, one would have to present a patent application containing results from *in vivo* human trials. This clearly is not the standard set forth by the Patent Office, as such a requirement would require extensive and unethical testing in humans. Indeed, this has been recognized in a number of U.S. Patents that have issued having claims directed towards methods of treatment wherein the examples did not include *in vivo* human results. For example, the Examiner is invited to review U.S. Patent Number 5,281,587, wherein method of treatment claims were allowed without the presence of *in vivo* human examples.

Additionally, Applicants respectfully assert that *in vitro* testing of compounds on human cancer cells is widely taught and is accepted in the art as a suitable alternative to widescale testing of compounds in humans. For example, the National Cancer Institute's Developmental Therapeutics Program maintains, *inter alia*, an *in vitro* screening program that is available to both academia and industry to identify compounds to be developed into therapeutic agents and treatments that uses 60 human tumor cell lines.

Furthermore, Applicants respectfully request that the Examiner review the enclosed article entitled "Clinical Predictive Value of the *in Vitro* Cell Line, Human Xenograft, and Mouse Allograft Preclinical Cancer Models" wherein it was determined through a retroactive review of the literature that *in vitro* cell line models were, in fact, predictive of clinical results. Therefore, the present specification, which provides *in vitro* cell line examples, is clearly enabled.

Accordingly, as the *in vitro* cell line model is widely accepted in the art, and as the presence of working examples is not a requirement for the obtaining of method of treatment claims, reconsideration and withdrawal of the enablement rejections are respectfully requested.

VI. THE REJECTIONS UNDER 35 USC §112, 2nd PARAGRAPH ARE OVERCOME

Claims 4-7 were rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. The amendments to the claims herein have canceled claim 4, and have inserted the term "related" into claim 6, such that claim 6 now recites a tumour necrosis factor-related apoptosis inducing ligand receptor, for which TRAIL is the appropriate acronym. As the recitation of claim 4 has been introduced into claim 1, a similar amendment was also made therein. It is respectfully submitted that these amendments clarify that TRAIL is indicated in parenthesis as the acronym of the recited cytokine, such that the claims are now sufficiently definite.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph, are respectfully requested.

CONCLUSION

In view of the remarks and attachments herewith the application is in condition for allowance. Consideration and entry of this paper, favorable reconsideration of the application and prompt issuance of a Notice of Allowance, are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date and greatly appreciates the opportunity to discuss this application with the Examiner during the upcoming interview scheduled for May 25, 2005.

Respectfully submitted,
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